

REMARKS

Claims 1, 9-11, 13-17, 20-23, 25-28, 30-33, 37, 43, 44, 46-48, and 50 were pending. Applicants have herein amended claims 1, 9, 13, 14, 26, 30, and 31; and cancelled claim 32 without prejudice to future prosecution. Applicants' specification fully supports the amended claims, thus no new matter has been added.

Accordingly, claims 1, 9-11, 13-17, 20-23, 25-28, 30, 31, 33, 37, 43, 44, 46-48, and 50 are pending. In light of the amendments and remarks herein, Applicants respectfully request reconsideration and allowance of the pending claims.

Telephonic Interview

Applicants wish to thank the Examiner for the telephonic interview of March 19, 2011 where the rejections under 35 U.S.C. § 112, first paragraph were discussed. No agreement as to the allowance of any claim was reached.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1, 9, 14-17, 20-23, 25, 26, 31-33, 43, 44, 46-48, and 50 under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. The Examiner conceded that the methods of making the claimed compounds are enabled by Applicants' specification (see Office Action at page 2), but asserted that the guidance provided by the specification in terms of enhancing cellular uptake at target cells invites further experimentation.

Applicants' respectfully disagree. The test of enablement is whether the specification teaches one skilled in the art how to make and use the full scope of the claimed invention without *undue experimentation*. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993) (emphasis added). Thus, the enablement analysis must be focused on the product or method defined by the claims. Importantly, "a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the

enabling requirement of the first paragraph *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.” *In re Marzocchi*, 439 F.2d 220, 222-223 (CCPA 1971) (emphasis in the original). The Examiner bears the burden of “providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement.” *In re Wright*, 999 F.2d at 1561 (Fed. Cir. 1993). The Examiner has not met her burden in the present case.

Applicants’ claims relate to compositions comprising a therapeutically active compound, selected from the group consisting of a nucleic acid, nucleoside, protein, peptide, amino acid residue, and dye, covalently bound to a guanidinoaminoglycoside and methods of increasing cellular uptake of a therapeutically active compound by administration of such compositions. Contrary to the Examiner’s assertions, Applicants’ specification provides sufficient disclosure to teach one skilled in the art how to *make and use* the full scope of the claimed invention without undue experimentation. The Examiner asserted that Applicants’ working examples are limited to the conjugation of a single therapeutic agent to a guanidinoaminoglycoside, but such is not the case. Applicants’ specification provides for the synthesis and characterization of guanidinoaminoglycosides conjugated to BODIPY (see Example 4 and 10), fluorescein (see Example 8 and 10) and AZT-monophosphate (see Example 11). Moreover, Applicants’ fully describe the conjugation of nucleoside reverse transcriptase inhibitors for use in the treatment of HIV. See FIG. 1 and [0044] – [0058]. These examples provide a variety of structural formulas and sizes to exhibit the effectiveness of conjugation to guanidiniaminoglycosides to increase cellular uptake of the conjugated active compounds.

Regarding the composition claims, the standard of enablement as described in § 2164.01 of the MPEP is that of a “practical utility.” Specifically, “[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim—the enablement standard is met.” MPEP § 2164.01. Applicants’ specification provides for increased cellular uptake as well as numerous additional uses for the claimed compositions. For example, the conjugates are useful in the delivery of therapeutic compounds, for treating patients suffering from various maladies, and as a method

for administering therapeutically active compounds. See [0020], [0042], [0066], and [0068]. Administration and use of the claimed therapeutically active compounds is well within the skill of one of the art. Accordingly, the enablement standard for the claimed compositions is clearly met.

Furthermore, the Office Action states that an enormous amount of trial and error to test various compounds encompassed by the claims would be required as there is no way to predict the cellular uptake of the compounds. As stated in the M.P.E.P. § 2164.06, the test for enablement is “not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.” *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)). The specification of the present application provides such guidance. Example 11 of the present application describes a method of evaluating the AZT-guanidino-neomycin B conjugate for increased cellular uptake. Moreover, it is known to one of ordinary skill in the art that labeling experiments would also reveal this information. Suitable labels, methods of producing labeled conjugates, and tools for analyzing labeling experiments are provided in paragraphs [0072] to [0074]. Example 10 also provides examples of multiple methods for evaluating cellular uptake of compounds. Per MPEP § 2164.01, the test of enablement is not whether any experimentation is necessary but whether, if experimentation is necessary, it is undue. The evaluation of guanidinoaminoglycosides covalently bound to a nucleic acid, nucleoside, protein, peptide, amino acid residue, or a dye involves experimentation that is routine to those of skill in the art. Thus, given Applicants’ disclosure and their base of knowledge, one of skill in the art would know how to make and/or use the full scope of the claims without undue experimentation.

In summary, the present claims are enabled by the specification as filed. Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

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Allowed Claims

Applicants respectfully acknowledge the allowance of claims 10, 11, 13, 27, 28, and 30.

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CONCLUSIONS

Applicant submits that claims 1, 9-11, 13-17, 20-23, 25-28, 30, 31, 33, 37, 43, 44, 46-48, and 50 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned at the telephone number below if such will advance prosecution of this application.

Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

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